

SEQUENCE LISTING

<110> BRASLAWSKY, GARY R.
HANNA, NABIL
HARIHARAN, KANDASAMY
LABARRE, MICHAEL J.
HUYNH, TRI B.



<120> PRODUCTION OF TETRAVALENT ANTIBODIES

<130> 23522.0584

<140> 09/238,741

<141> 1999-01-28

<150> 4

<170> PatentIn Ver. 2.1

<210> 1

<211> 708

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: DNA encoding
"Dimeric" Anti-CD20 Light Chain (Version 1)

<220>

<221> CDS

<222> (1)..(705)

<400> 1

atg gat ttt cag gtg cag att atc agc ttc ctg cta atc agt gct tca	48
Met Asp Phe Gln Val Gln Ile Ile Ser Phe Leu Leu Ile Ser Ala Ser	
1 5 10 15	
gtc ata atg tcc aga gga caa att gtt ctc tcc cag tct cca gca atc	96
Val Ile Met Ser Arg Gly Gln Ile Val Leu Ser Gln Ser Pro Ala Ile	
20 25 30	
ctg tct gca tct cca ggg gag aag gtc aca atg act tgc agg gcc agc	144
Leu Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg Ala Ser	
35 40 45	
tta agt gta agt tac atc cac tgg ttc cag cag aag cca gga tcc tcc	192
Ser Ser Val Ser Tyr Ile His Trp Phe Gln Gln Lys Pro Gly Ser Ser	
50 55 60	
ccc aaa cgc tgg att tat gcc aca tcc aac ctg gct tct gga gtc cct	240
Pro Lys Arg Trp Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro	
65 70 75 80	
gtt cgc ttc agt ggc agt ggg tct ggg act tct tac tct ctc aca atc	288
Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Thr Ser Leu Thr Ile	

agc aga gtg gag gct gaa gat gct gcc act tat tac tgc cag cag tgg 336
 Ser Arg Val Glu Ala Glu Asp Ala Thr Tyr Tyr Cys Gln Gln Trp
 100 105 110

act agt aac cca ccc acg ttc gga ggg ggg gcc aag ctg gaa atc aaa 384
 Thr Ser Asn Pro Pro Thr Phe Gly Gly Gly Ala Lys Leu Glu Ile Lys
 115 120 125

cgt acg gtg gct gca cca tct gtc ttc atc ttc ccg cca tct gat gag 432
 Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
 130 135 140

cag ttg aaa tct gga act gcc tct gtt gtg tgc ctg ctg aat aac ttc 480
 Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
 145 150 155 160

tat ccc aga gag gcc aaa gta cag tgg aag gtg gat aac gcc ctg cca 528
 Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
 165 170 175

tgg ggt aac tcc cag gag agt gtc aca gag cag gac agc aag gac agc 575
 Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
 180 185 190

acc tac agc ctg agc agc acc ctg acg ctg agc aaa gca gac tac gag 624
 Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
 195 200 205

aaa cac aaa gtc tac gcc tgc gaa gtc acc cat cag gcc ctg agc tgc 672
 Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
 210 215 220

ccc gtc aca aag agc ttc aac agg gga gag tgt tga 708
 Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230 235

<210> 2

<211> 235

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:

"Dimeric" Anti-CD20 Light Chain (Version 1)

<400> 2

Met Asp Phe Gln Val Gln Ile Ile Ser Phe Leu Leu Ile Ser Ala Ser
 1 5 10 15

Val Ile Met Ser Arg Gly Gln Ile Val Leu Ser Gln Ser Pro Ala Ile
 20 25 30

Leu Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Arg Ala Ser
 35 40 45

Pro Lys Arg Trp Ile Tyr Ala Thr Ser Asn Leu Ala Ser Gly Val Pro
 65 70 75 80
 Val Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile
 85 90 95
 Ser Arg Val Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp
 100 105 110
 Thr Ser Asn Pro Pro Thr Phe Gly Gly Gly Ala Lys Leu Glu Ile Lys
 115 120 125
 Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
 130 135 140
 Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
 145 150 155 160
 Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
 165 170 175
 Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
 180 185 190
 Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
 195 200 205
 Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
 210 215 220
 Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
 225 230 235

<210> 3
 <211> 1413
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: DNA encoding
 "Dimeric" Anti-CD20 Heavy Chain (Version 1)

<220>
 <221> CDS
 <222> (1)..(1410)

<400> 3
 atg ggt tgg agc ctc atc ttg ctc ttc ctt gtc gct gtt gct acg cgt 48
 Met Gly Trp Ser Leu Ile Leu Leu Phe Leu Val Ala Val Ala Thr Arg
 1 5 10 15

gta atg tgg cag gta cag atg cag cag cgt ggt ggt ggt ggt ggt ggt 49

cct ggg gcc tca gtg aag atg tcc tgc aag gct tct ggc tac aca ttt	144
Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe	
35 40 45	
acc agt tac aat atg cac tgg gta aaa cag aca cct ggt cgg ggc ctg	192
Thr Ser Tyr Asn Met His Trp Val Lys Gln Thr Pro Gly Arg Gly Leu	
50 55 60	
gaa tgg att gga gct att tat ccc gga aat ggt gat act tcc tac aat	240
Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn	
65 70 75 80	
cag aag ttc aaa ggc aag gcc aca ttg act gca gac aaa tcc tcc agc	288
Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser	
85 90 95	
aca gcc tac atg cag ctc agc agc ctg aca tct gag gac tct gcg gtc	336
Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val	
100 105 110	
tat tac tgt gca aga tcg act tac tac ggc ggt gac tgg tac ttc aat	384
Tyr Tyr Cys Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn	
115 120 125	
gtc tgg ggc gca ggg acc acg gtc acc gtc tct gca gct agc acc aag	432
Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ala Ala Ser Thr Lys	
130 135 140	
ggc cca tcg gtc ttc ccc ctg gca ccc tcc tcc aag agc acc tct ggg	480
Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly	
145 150 155 160	
ggc aca gcg gcc ctg ggc tgc ctg gtc aag gac tac ttc ccc gaa ccg	528
Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro	
165 170 175	
gtg acg gtg tcg tgg aac tca ggc gcc ctg acc agc ggc gtg cac acc	576
Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr	
180 185 190	
ttc ccg gct gtc cta cag tcc tca gga ctc tac tcc ctc agc agc gtg	624
Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val	
195 200 205	
gtg acc gtg ccc tcc agc agc ttg ggc acc cag acc tac atc tgc aac	672
Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn	
210 215 220	
gtg aat cac aag ccc agc aac acc aag gtg gac aag aaa gtt gag ccc	720
Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro	
225 230 235 240	
aaa tct tgt gac aaa act cac aca tgc cca ccg tgc cca gca cct gaa	768
Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu	
245 250 255 260	

ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac	816
Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp	
260 265 270	
acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac	864
Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp	
275 280 285	
gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc	912
Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly	
290 295 300	
gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac	960
Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn	
305 310 315 320	
agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg	1008
Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp	
325 330 335	
ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca	1056
Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro	
340 345 350	
gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa	1104
Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu	
355 360 365	
cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac	1152
Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn	
370 375 380	
cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc	1200
Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile	
385 390 395 400	
gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc	1248
Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr	
405 410 415	
acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag	1296
Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys	
420 425 430	
ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc	1344
Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys	
435 440 445	
tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc	1392
Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu	
450 455 460	
tcc ctg tgt ccg ggt aaa tga	1413
Ser Leu Cys Pro Gly Lys	

<210> 4
 <211> 470
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:
 "Dimeric" Anti-CD20 Heavy Chain (Version 1)

<400> 4

```

Met Gly Trp Ser Leu Ile Leu Leu Phe Leu Val Ala Val Ala Thr Arg
 1              5              10              15

Val Leu Ser Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys
      20              25              30

Pro Gly Ala Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe
      35              40              45

Thr Ser Tyr Asn Met His Trp Val Lys Gln Thr Pro Gly Arg Gly Leu
      50              55              60

Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn
      65              70              75              80

Gln Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser
      85              90              95

Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val
      100             105             110

Tyr Tyr Cys Ala Arg Ser Thr Tyr Tyr Gly Gly Asp Trp Tyr Phe Asn
      115             120             125

Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ala Ala Ser Thr Lys
      130             135             140

Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly
      145             150             155             160

Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
      165             170             175

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
      180             185             190

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
      195             200             205

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn
      210             215             220

Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro
      225             230             235             240

```

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
 260 265 270
 Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
 275 280 285
 Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
 290 295 300
 Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
 305 310 315 320
 Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
 325 330 335
 Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
 340 345 350
 Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
 355 360 365
 Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
 370 375 380
 Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
 385 390 395 400
 Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
 405 410 415
 Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
 420 425 430
 Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
 435 440 445
 Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
 450 455 460
 Ser Leu Cys Pro Gly Lys
 465 470